CLINICAL AND PHYSIOLOGIC IMPLICATIONS OF THALAMIC SURGERY FOR DYSTONIA AND TORTICOLLIS*

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It is a singular privilege to join Derek Denny-Brown in this seminar on the nature of dystonia. I should like to present some of the observations that we have made on patients with dystonia, torticollis, and certain related syndromes, who have undergone thalamic surgery for relief of their hyperkinetic syndromes. It is my hope that these observations incident to neurosurgical treatment of certain disorders of sensory communication may contribute to an elucidation of the abnormal mechanisms underlying their motor manifestations. In this regard, one of the major theses of this report is the fact that dystonia and torticollis, like intention tremor, appear to have some element of hyperkinesis induced by intention or voluntary movement. Each appears to have in common with intention tremor some involvement of the dentatorubrothalamocortico pathway, or fibers emerging from the emboliform nucleus traveling in the brachium conjunctivum to centrum medianum. Although the importance of the cerebellar mechanism in the production of pure intention tremor has been widely appreciated, its contribution to the mechanism of other hyperkinesis has not been stressed. It is the purpose of these remarks tonight to emphasize the contribution of abnormal sensory communication of the cerebellar pathways to the mechanism of these hyperkinetic syndromes.

DYSTONIA MUSCULORUM DEFORMANS

Our series of operations for dystonia musculorum deformans now numbers 130 cases.[1-6] These patients may be divided into three groups, dependent upon age at the onset of symptoms. The first group noted onset of dystonia prior to 12 years of age, and the third group had the

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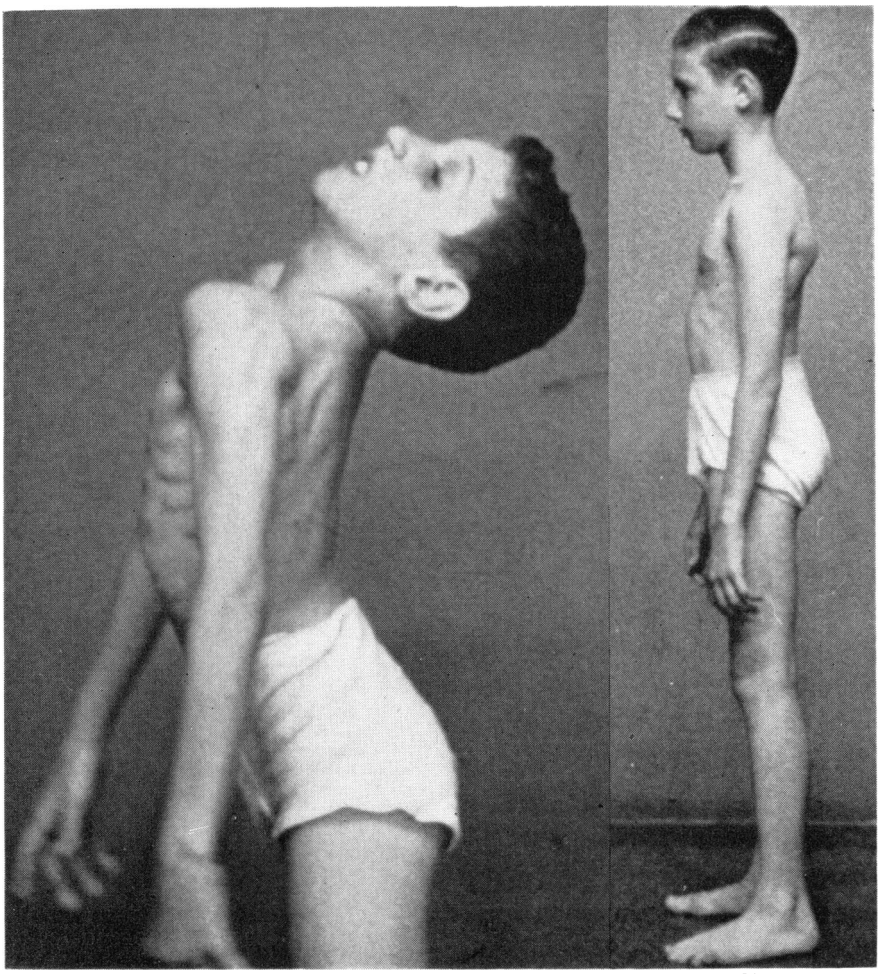
onset of symptoms over the age of 21 years. These two groups may be distinguished by the following criteria: about 50 per cent of the early age group were Jewish or had Jewish ancestry, as compared to only 20 per cent in the older age group. Moreover, two thirds of the patients with Jewish ancestry had a positive family history, whereas this was not obtained from patients of other ethnic origin. Scoliosis was about twice as frequent in the early age group, and torticollis was about twice as frequent in the older-age group. Facial involvement was about four times as frequent in the older-age group. In between these two rather well-defined groups of patients, there was a third group with the age of onset 13 to 20. These patients had a distribution of signs and symptoms that were intermediate in position between the two more clearly defined groups.

The pathogenetic lesions underlying dystonia musculorum deformans may be variably situated throughout the brain, but the principal causative lesions lie in the caudate nucleus and putamen and in the pathways from the dentate nucleus and brachium conjunctivum. Moreover, our own investigations have demonstrated that inhibition of the caudate nucleus, putamen, dentate nucleus, or posterior limb of the internal capsule invariably worsened dystonic symptoms.

Herz's definition of dystonia as a selective system symptomatalogy thus can be supported not only on a clinical basis, but probably also by reference to anatomic-pathologic criteria.[7] The pathogenesis of athetosis, on the other hand, generally involves not only lesions of the sensory circuits modifying cortical activity, but also widespread lesions of the cortex and its efferent tracks. Athetosis thus differs from dystonia in being superimposed upon, or concurrent with, hemiparesis and spasticity in most instances. This report deals specifically with dystonia and, more specifically, with that type seen in cases of dystonia musculorum deformans.

The principal result of this study is the fact that every observable dystonic hyperkinetic motion, posture, and deformity is potentially reversible by one or more deep intracerebral lesions. Its reversal may be obtained without infliction of any observable sensory, motor, or reflex abnormality. In some instances, such reversal was obtained by a single lesion in the globus pallidus, or in the ventrolateral nucleus of the thalamus. In most instances, however, double lesions were inflicted in each hemisphere. Among these cases, lesions placed in the following



(*a*) (*b*)

Fig. 1. (*a*) Eleven-year-old boy totally incapacitated by opisthotonic dystonia.

(*b*) Same patient two years following bilateral thalamic surgery. Patient is neurologically, intellectually, and psychologically normal.

sites have greatly relieved or abolished the dystonia: mesial globus pallidus, ventrolateral nucleus of the thalamus, zona incerta, centrum medianum, and posteroventrolateral and posteroventromedial nuclei. At the present time, on the basis of a detailed analysis of these cases, we have concluded that the lesion of choice is a comma-shaped, double lesion that involves the posterior half of the ventrolateral nucleus, the anterior portion of VPL and VPM, and the outer two thirds of the centrum medianum.

Slightly more than 70 per cent of our total series of dystonic cases have achieved long-standing abolition of their dystonia, as exemplified by the films previously seen. Moreover, the long-term follow-up of these patients demonstrates a remarkable resilience of the human brain (particularly the young human brain) to thalamic surgery. Not only have many of these previously totally incapacitated patients been restored to a state of virtual neurologic normality, but they have also continued to demonstrate a high degree of intelligence, along with remarkable emotional and psychologic behavior.

It is a remarkable fact that some of these youngsters have tolerated as many as six lesions in the thalamus, that is, three on each side of the brain, and not only have been relieved of hyperkinesis but have retained normal intellectual, psychologic, emotional, and sensory and motor function. The significance of this observation in humans as it relates to the basic physiologic function of the thalamus holds many implications that are yet not entirely explained.

Representative cases are illustrated in Figures 1 to 6.

In regard to bilateral surgery in cases of dystonia, as well as of certain other hyperkinesis, it should be pointed out that in most instances, particularly as regards the extremities, the effect of thalamic surgery is observed principally contralateral to the side of surgery. However, this is not invariably the case, and the relationship of the two hemispheres as related to the physiology of sensory communication from one side of the body and to the mechanisms underlying dystonic and related hyperkinesis is not yet clear. Certain electromyographic observations are of interest in this regard.

Figure 7 demonstrates the typical abnormality of dystonia musculorum deformans. The preoperative slide demonstrates the fact that voluntary motion of an extremity in a dystonic is characterized by concerted action of the antagonists at the same time. The postoperative slide demonstrates quite clearly the fact that successful alleviation of the dystonia enables the patient voluntarily to contract the antagonists alternately. Thus the basic mechanism underlying dystonia, namely the tendency of antagonistic muscles to contract simultaneously, is alleviated by thalamic surgery. In this instance, the lesions were placed in the ventrolateral (VL), ventroposterolateral (VPL), ventroposteromedial (VPM), and centrum medianum nuclei of the thalamus.

Severe involuntary contractions in the foreleg, produced by an

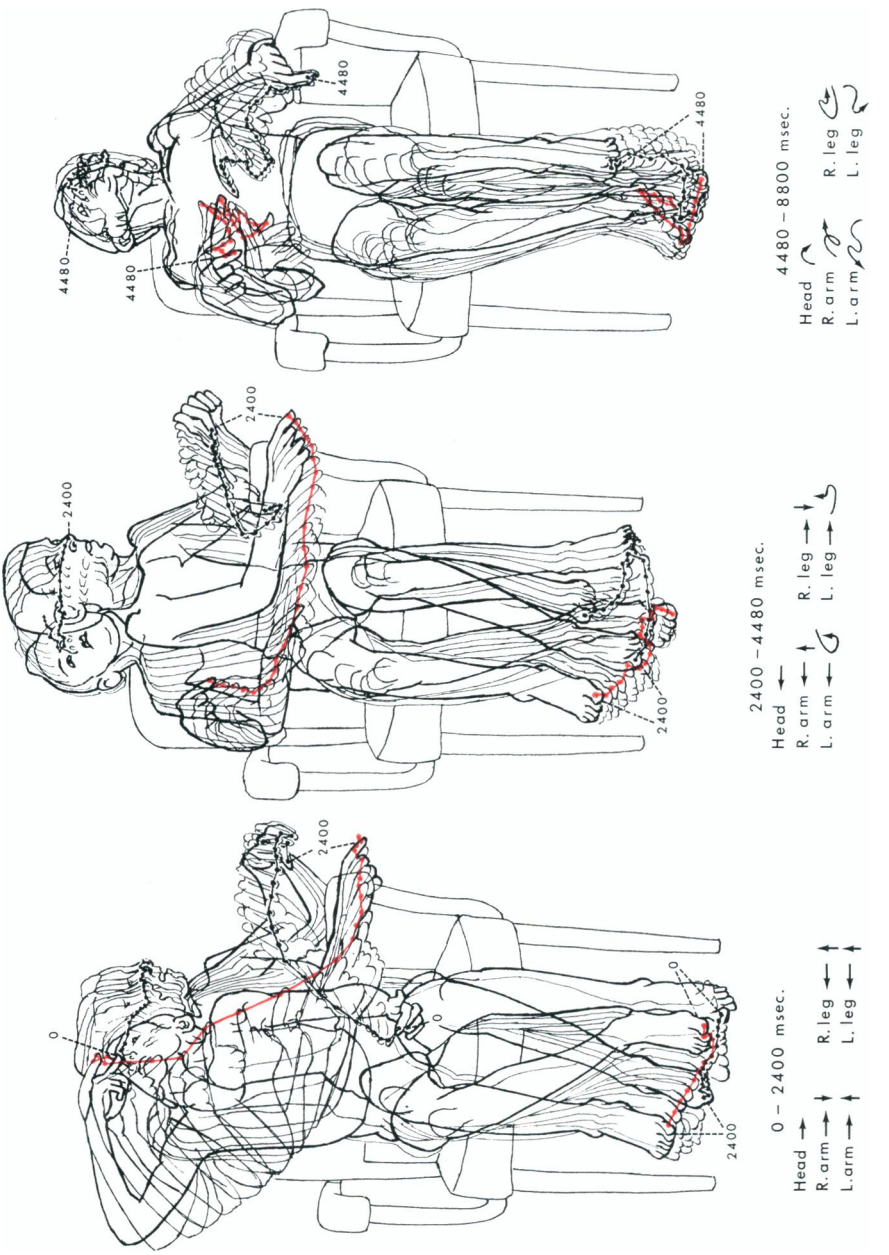
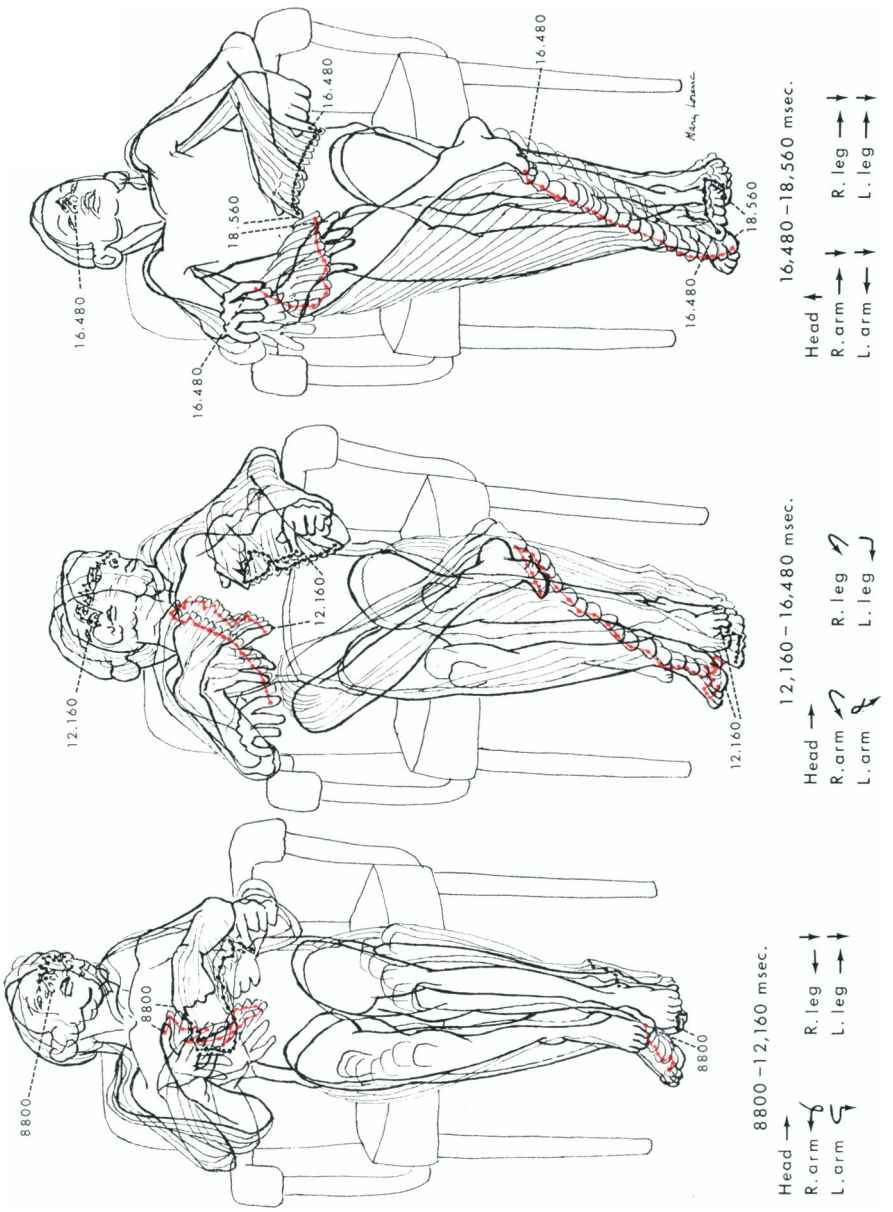


Fig. 2. Serial tracings of cinematographic record demonstrating involuntary movements in an 11-year-old boy with dystonia pictured in Figure 1. Red and black lines illustrate the chain of involuntary movements triggered when the patient voluntarily attempted



the finger-to-nose test. This resulted in the afterdischarge of involuntary movements of the entire body as the patient attempted to return his hand to the starting position. The importance of proprioceptive stimuli in the production of the hyperkinesis of dystonia is clearly evident.

Fig. 3 Serial tracings from cinematographic record pre- and postoperatively to illustrate the necessity of bilateral thalamic surgery for dystonia.
(*a*) Severe bilateral intention tremor and torticollis which was present preoperatively.

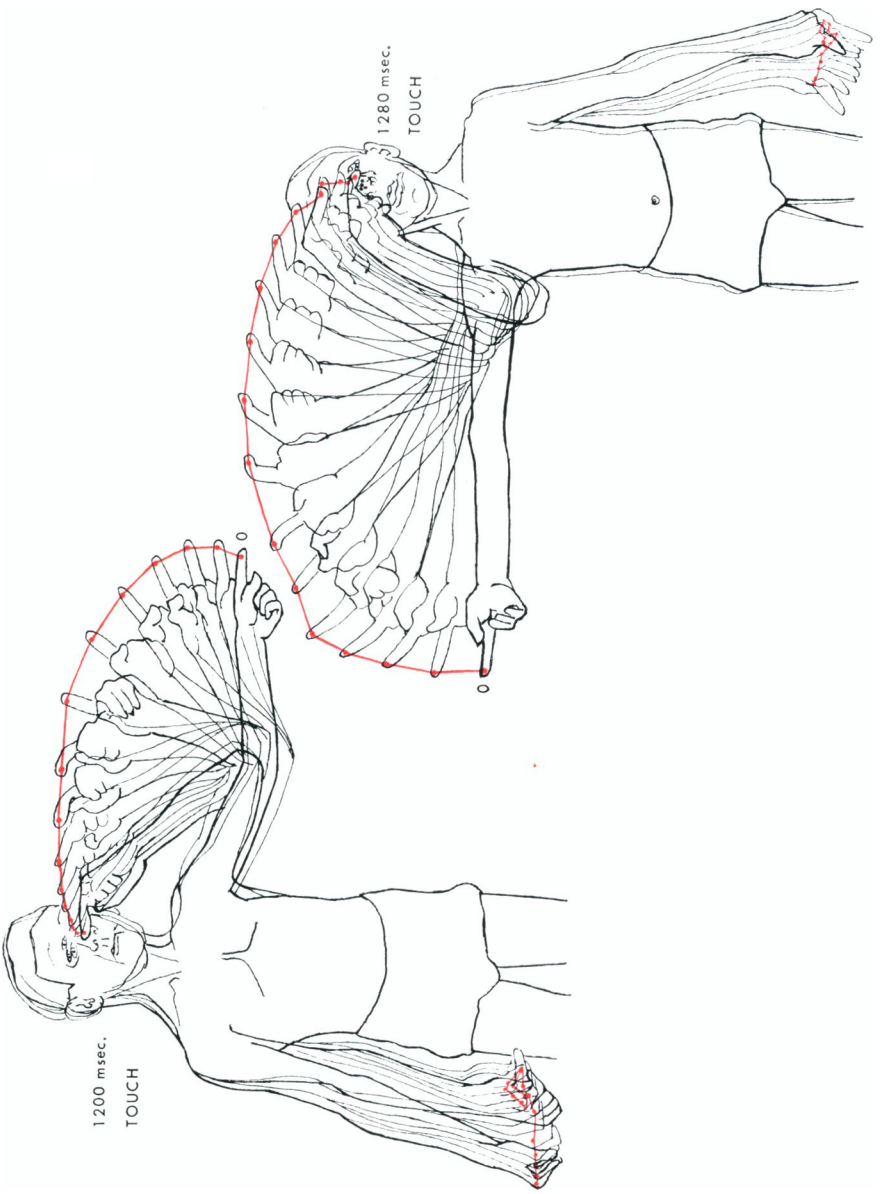


Fig. 3 (*b*) The same patient 12 months after right thalamic surgery. The left extremities are virtually normal, and the retrocollis is markedly improved. However, in addition to the right-sided involuntary movements, slight tremor of the left hand is produced during voluntary motions of the right upper extremity.

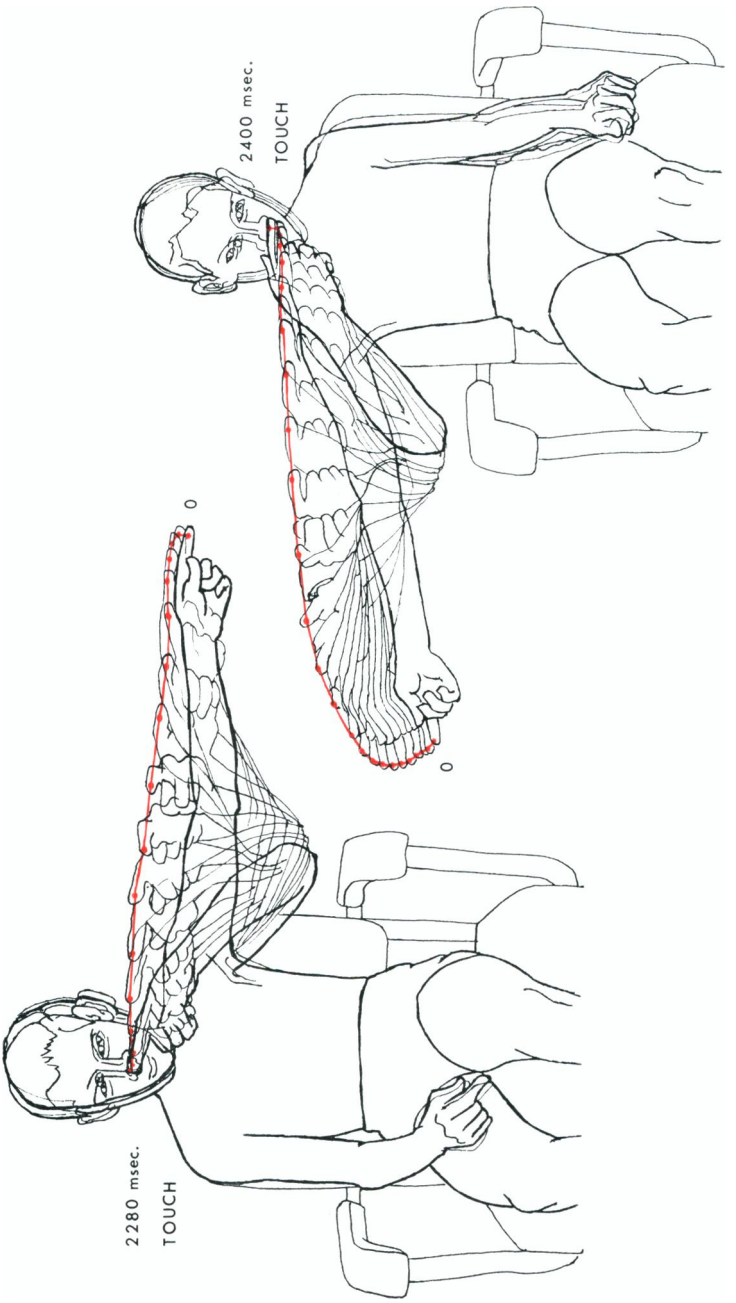
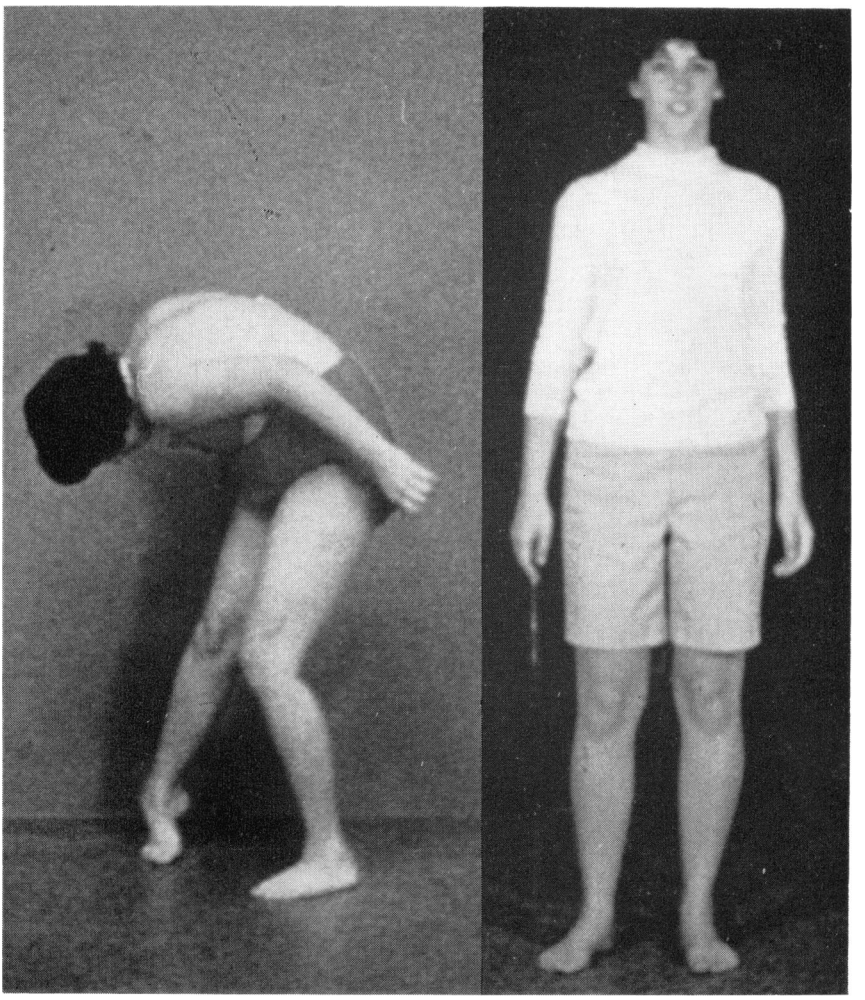


Fig. 3 (*c*) One year following bilateral thalamic surgery, involuntary movements on both sides of the body are abolished. Thus a second or left-sided thalamic operation is observed to have an ipsilateral as well as contralateral effect.



(*a*) (*b*)

Fig. 4 (*a*) Severe torsion spasm of dystonia musculorum deformans in a 13-year-old girl.

(*b*) The same patient eight years following bilateral thalamic surgery. She appears to be neurologically and intellectually normal.

attempt to elevate the lower extremity at the hip is illustrated by the electromyographic tracing in Figure 8. Such contractions in the foreleg are not seen in a normal individual during this movement. A postoperative film demonstrates the same ability of the patient to perform the same movement without the production of involuntary contractions.

One observes the fairly typical effect of a unilateral lesion upon bilateral dystonia in Figure 9. The preoperative film demonstrates

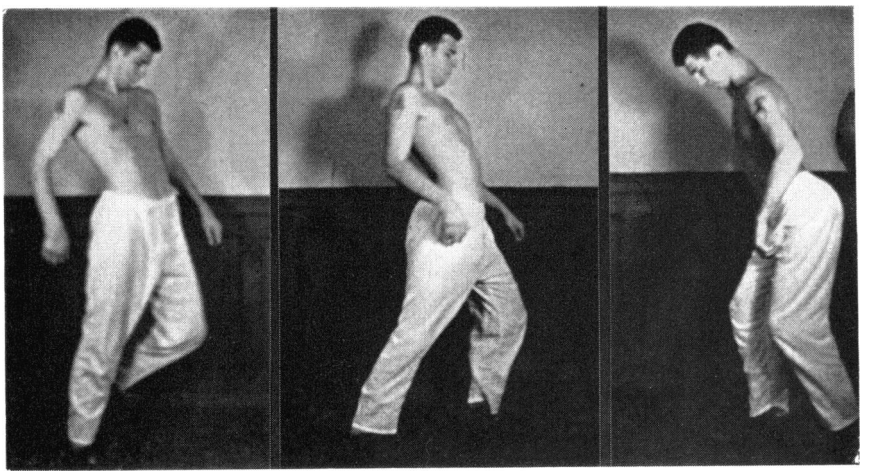


Fig. 5 (*a*) Severe truncal dystonia in a 24-year-old man.

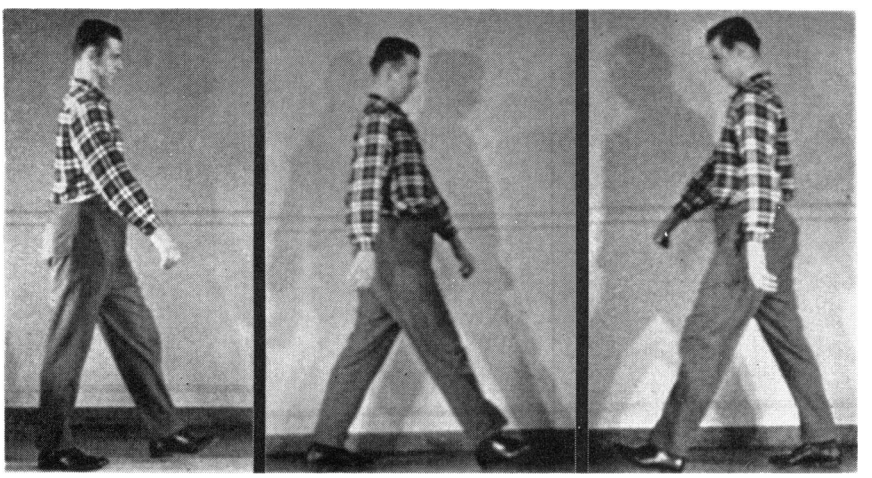


Fig. 5 (*b*) Same patient seven years following bilateral thalamic surgery.

obvious bilateral involvement. The immediate postoperative film demonstrates the fact that a lesion in the right VL and VPL nuclei have had an ameliorating effect upon involuntary movements on both sides of the body. However, a long-range postoperative follow-up tracing demonstrates that the left, that is, the side contralateral to surgery, remains alleviated of dystonic hyperkinesis, while the right side, or the side ipsilateral to surgery, has relapsed. Surgery on the left side of the brain subsequently relieved this side also.

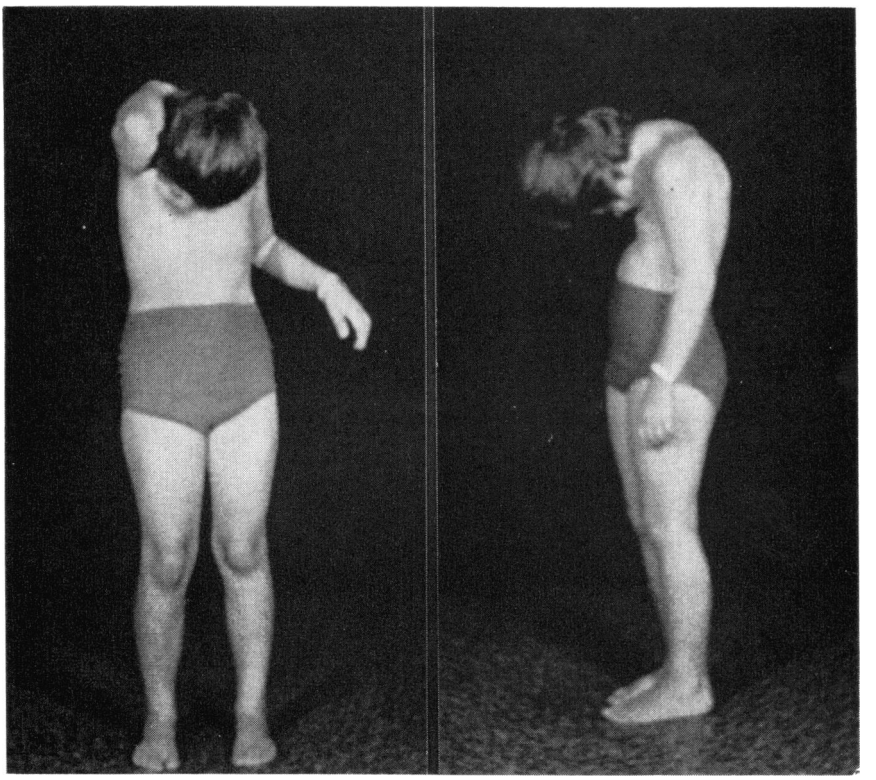


Fig. 6 (*a*) Eight-year-old girl with rapidly progressive dystonia affecting particularly the right upper extremity, the head, and the neck.

The chain of events that would lead to immediate suppression of bilateral involuntary activity, with recurrence on the ipsilateral side, deserves further elucidation.

On the other hand, as illustrated by a case of Wilson's disease, represented in Figures 10 to 12, a single unilateral lesion in rare instances may have a profound lasting bilateral effect. This case of a totally incapacitated 28-year-old female demonstrates the immediate bilateral abolition of involuntary movement of the sternocleidomastoid muscles on each side of the body, following the placement of the VL-VPL-VPM lesion on one side. The remarkable bilateral effect in this case was demonstrated clinically in the motion picture film. Its verification is clear in the diagrammatic composition of the film record.

Apparently lesions within the caudate nucleus, putamen, dentate nucleus, or brachium conjunctivum interfere with sensory communication from the external environment, from the muscles themselves, and

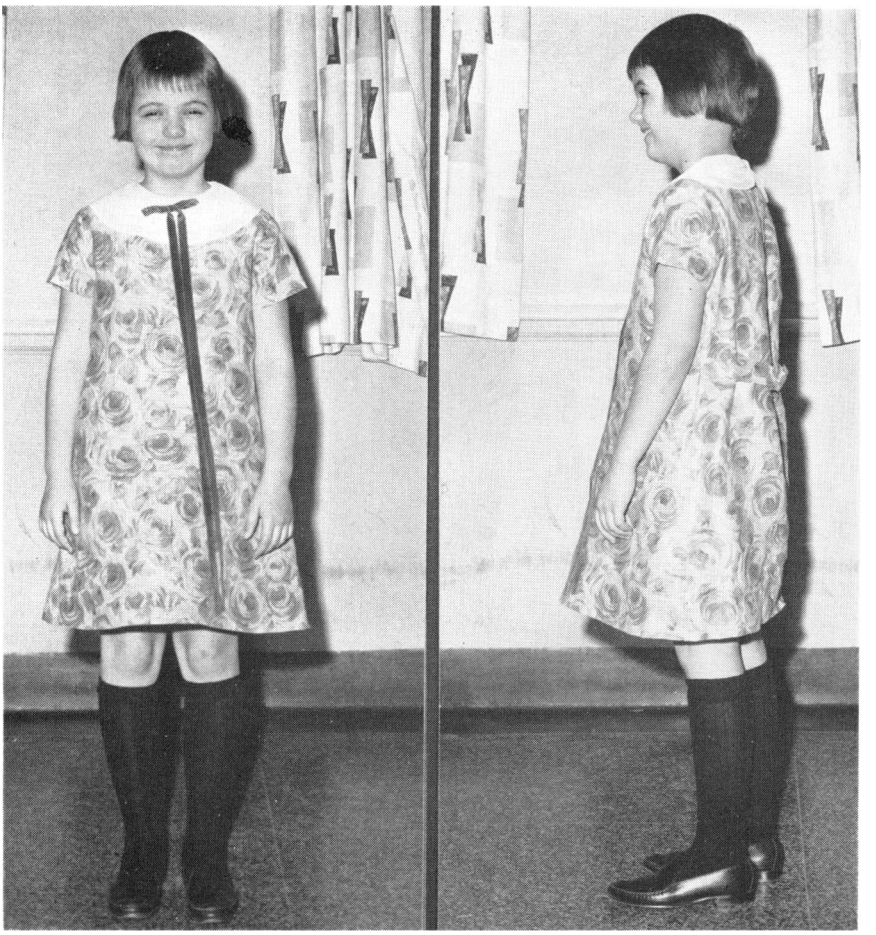


Fig. 6 (*b*) The same child one year following successful cryothalamectomy.

from other sensory stimuli which help to modulate normal motor activity. An abnormal synchronization of these modulating influences appears to be an important factor in the production of dystonia. Almost all of these feedback circuits converge in the lateral thalamus and centrum medianum en route to the motor cortex. Since this convergence is essential to the integrated action of the central nervous system, an abnormal synchronization of these feedback influences is reflected in dystonic movements, many of which are initiated by intention or posture. Especially at the onset of the disease, the dystonic responses appear to be secondary to voluntary movements of the extremities and are aggravated or facilitated by diverse proprioceptive or loading stimuli.

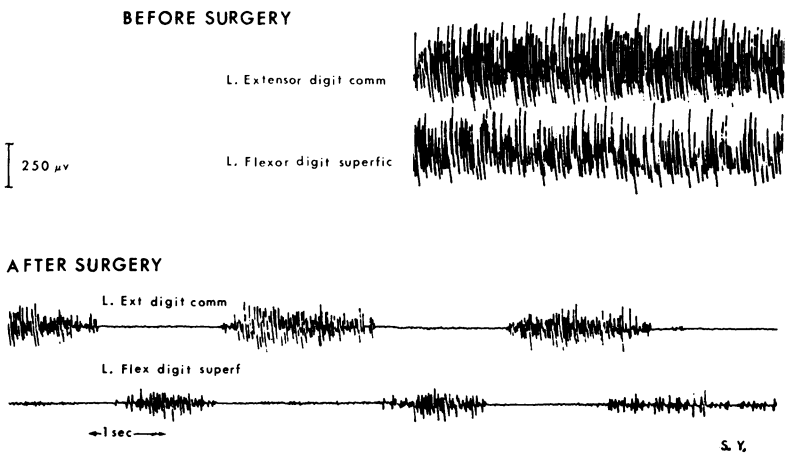


Fig. 7. Electromyographic tracing demonstrating the typical simultaneous contraction of antagonistic muscles in a patient with dystonia musculorum deformans prior to surgery. The lower two tracings demonstrate the ability of this patient to flex and extend the wrist normally, with restoration of inhibition of antagonistic muscles during the contraction of the protagonist, following thalamic surgery. These tracings made before and after thalamic surgery in a patient with dystonia musculorum deformans demonstrate that thalamic surgery abolishes the basic pathologic mechanism of dystonia, namely, simultaneous contraction of antagonistic muscles.

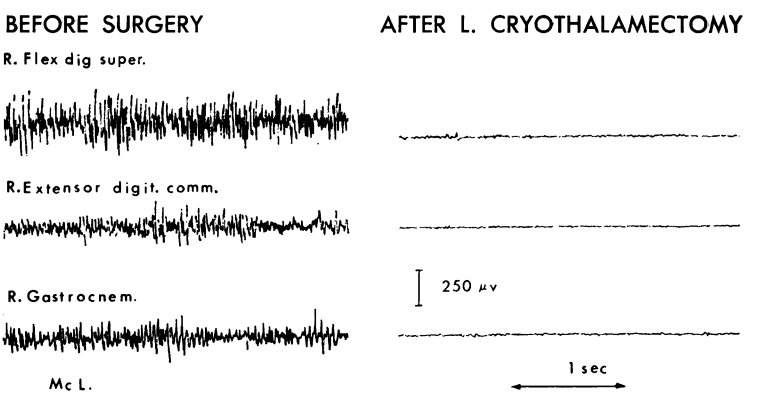


Fig. 8. Electromyogram demonstrating dystonic contraction of muscles in the right extremity when the patient attempted to elevate this extremity at the hip. Following left cryothalamectomy this abnormal discharge is not observed in the electromyogram.

Torticollis

During the past 10 years we have operated upon 90 patients with torticollis or retrocollis, which appeared as solitary symptoms or, in a few instances, as part of a more generalized dystonic syndrome. It is my opinion that torticollis is a syndrome of nuchal hyperkinesis that is organically determined, and I believe it should be considered a variant

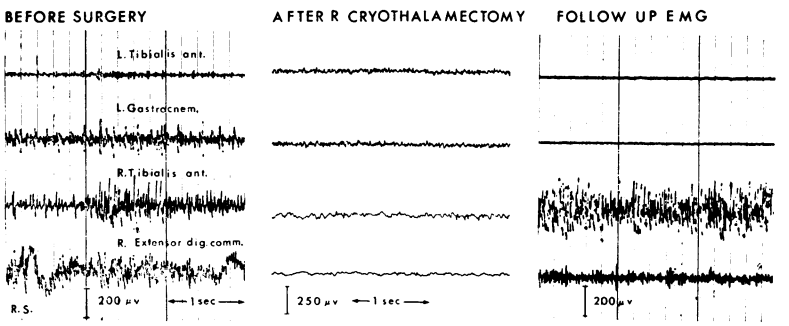
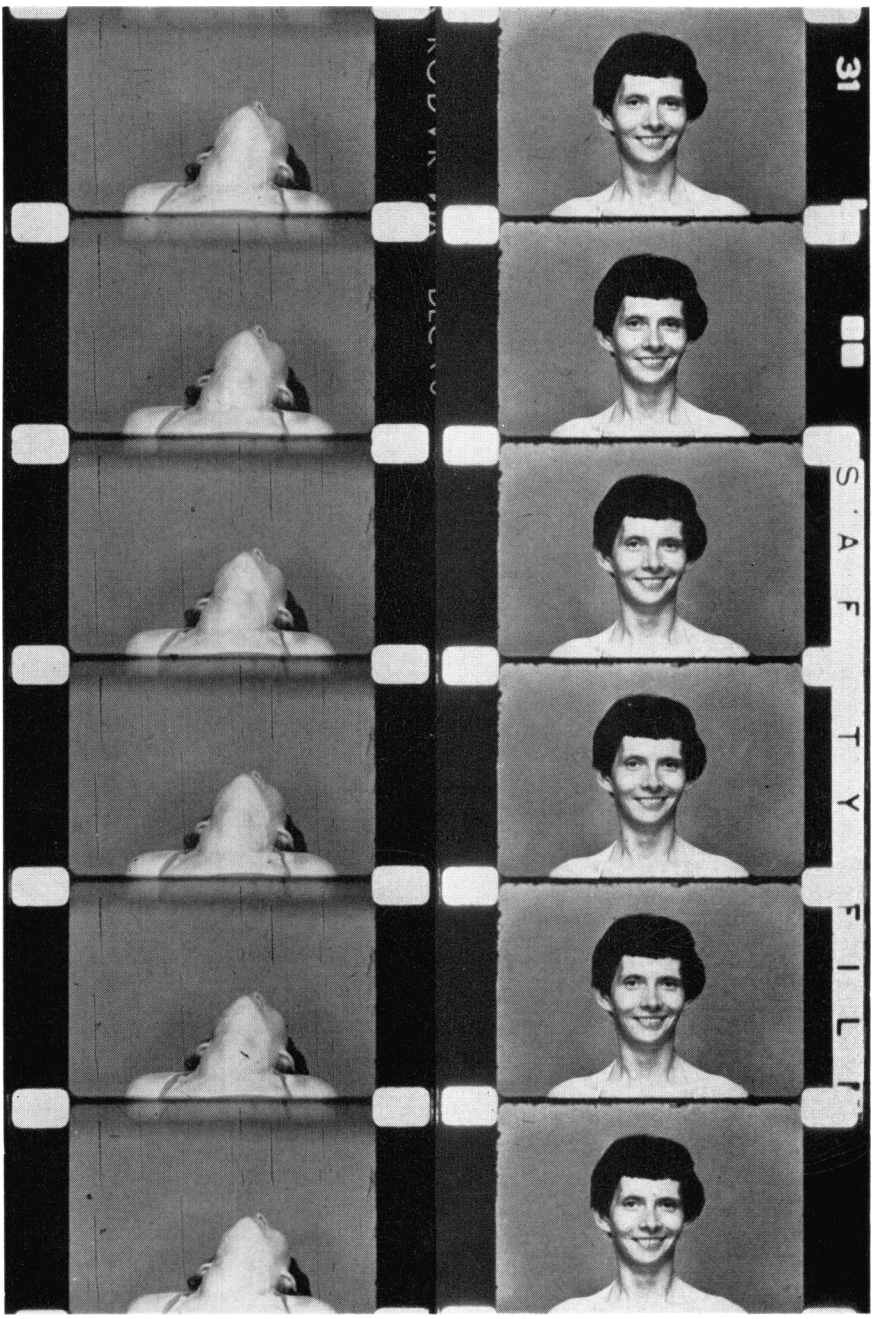


Fig. 9. Electromyographic tracings demonstrating ipsilateral and contralateral effects of thalamic lesions in dystonia. This series of tracings demonstrates that immediately following a right cryothalamectomy involuntary muscular activity was abolished in the lower extremities of both sides. However, the follow-up electromyogram demonstrates that six months following surgery, although the dystonic muscular activity was still abolished in the left lower extremity contralateral to surgery, the ipsilateral muscular contractions had recurred. These were subsequently abolished by a right cryothalamectomy.

It is not uncommon to note an ipsilateral effect of thalamic surgery in certain cases of dystonia. However, in most instances the ipsilateral effect is a minor one or, in those cases in which it is marked immediately following surgery, it usually regresses with the passage of time. Only rarely does a profound ipsilateral effect of thalamic surgery endure. However, the contralateral effect is usually lasting, even in those cases in which the ipsilateral effect may not be.

of dystonia. The production of rotary head movements in cats by stimulation of the nucleus interstitialis by Jung and Hassler,[8] experimental development of similar involuntary movements of the head and neck by stimulation of midline cerebellar nuclei,[9] and the fact that a lesion affecting the brachium conjunctivum and mesencephalic tegmentum can produce a torticollislike syndrome in laboratory animals,[10] provide evidence that the cerebellothalamic connections traveling via the brachium conjunctivum either directly, or through the red nucleus to the thalamus, subserve at least part of the pathophysiologic mechanism of torticollis.

Clinical evidence supporting this conclusion may be derived from the fact that torticollis is often accompanied by intention tremor of one or both upper extremities. Furthermore, the fact that abnormal posture and involuntary movements of the head and neck in many cases of torticollis appear to be determined by intention on the part of the patient and may be relieved when the muscles are totally at rest likewise suggest that an abnormality of the cerebellar servomechanism involving the cerebellothalamocortico circuits probably contribute to the nuchal hyperkinesis constituting the torticollis syndrome.



(*a*) (*b*)

Fig. 10. (*a*) Cinematographic record of severe retrocollis in a 27-year-old woman with Wilson's disease.

(*b*) Same patient four years following left thalamic surgery. The marked bilateral effect of the left thalamic lesion upon severe retrocollis is unique in this series.

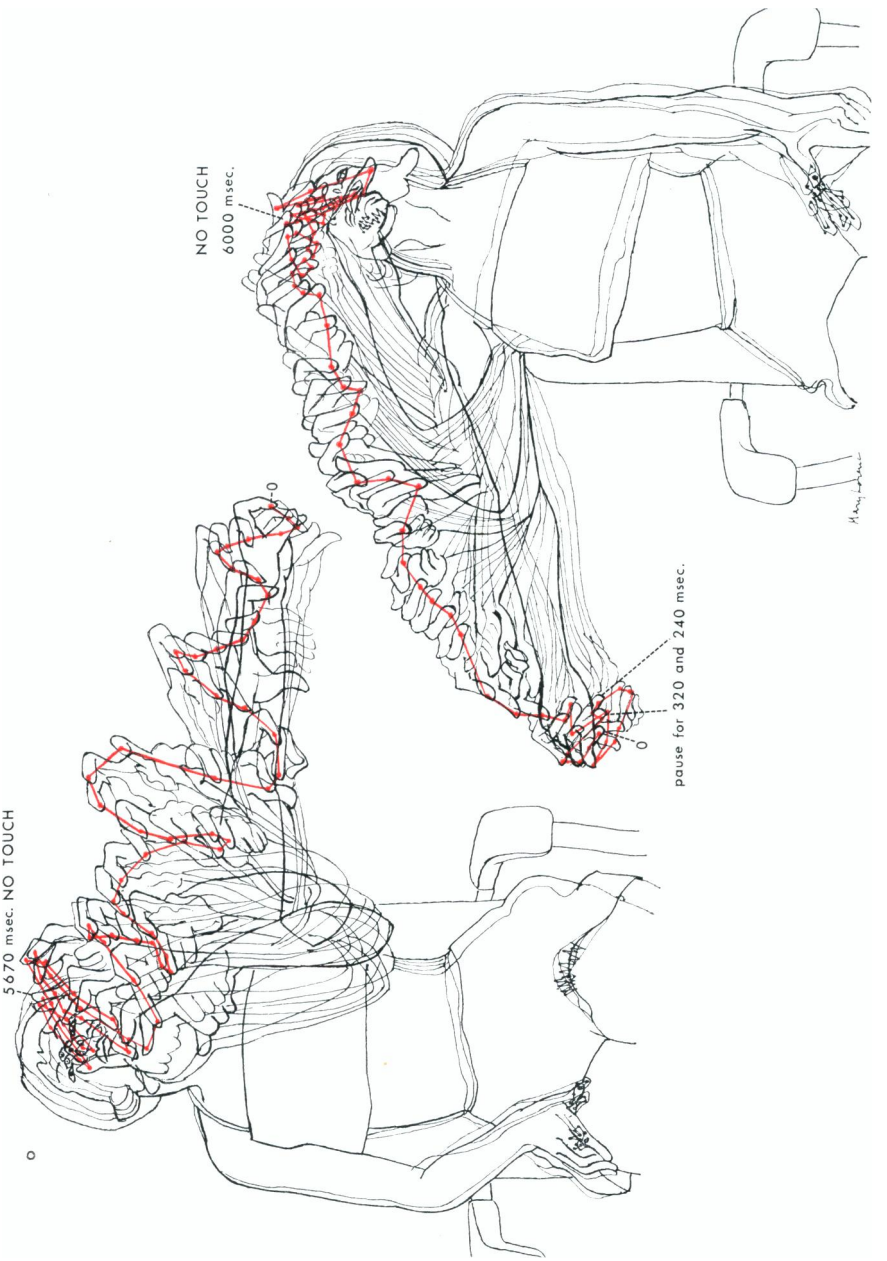


Fig. 11. (*a*) Tracings of cinematographic record of attempted finger-to-nose test in a 27-year-old woman with Wilson's disease. This severe intention tremor exacerbates the patient's retrocollis, and induces involuntary movements in all extremities.

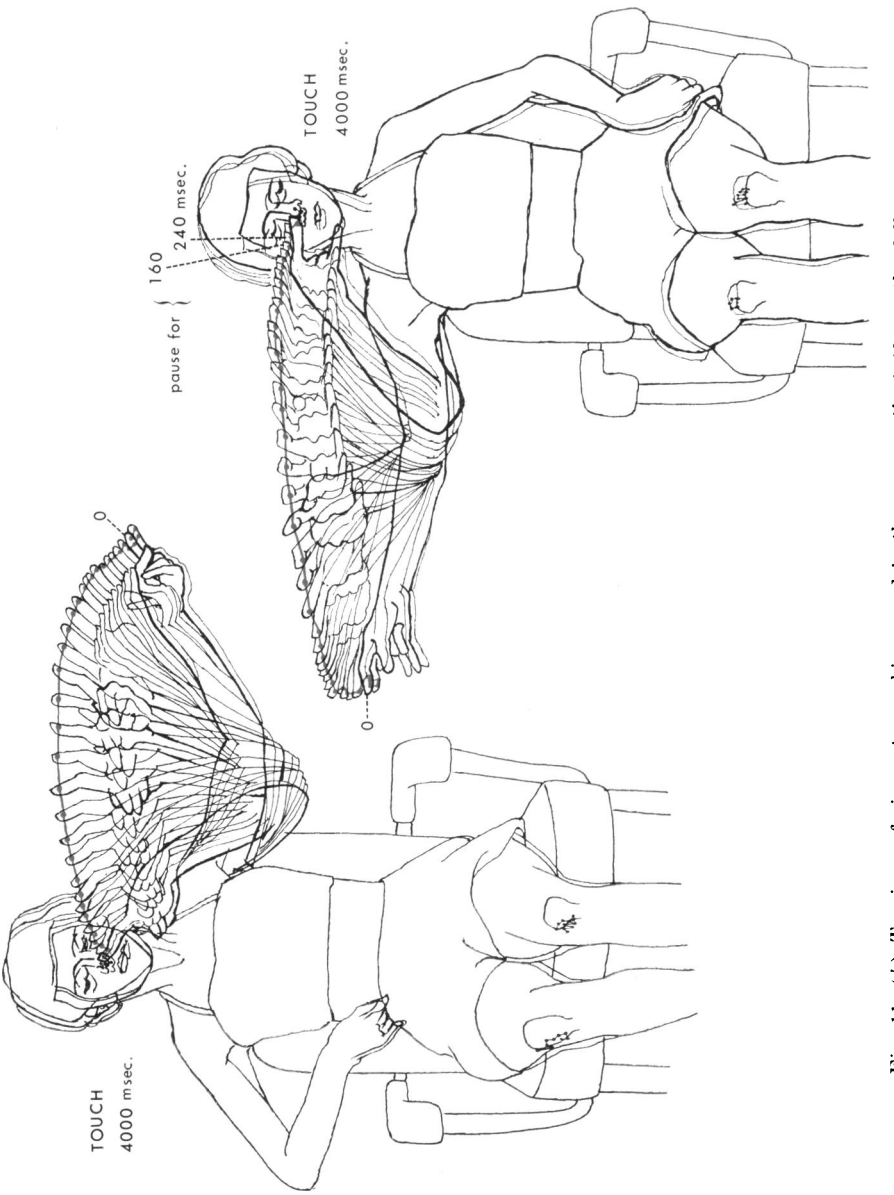


Fig. 11. (*b*) Tracings of cinematographic record in the same patient 10 months following left chemothalamectomy. In this case there was a profound favorable effect upon the involuntary movements of the ipsilateral as well as contralateral extremities.

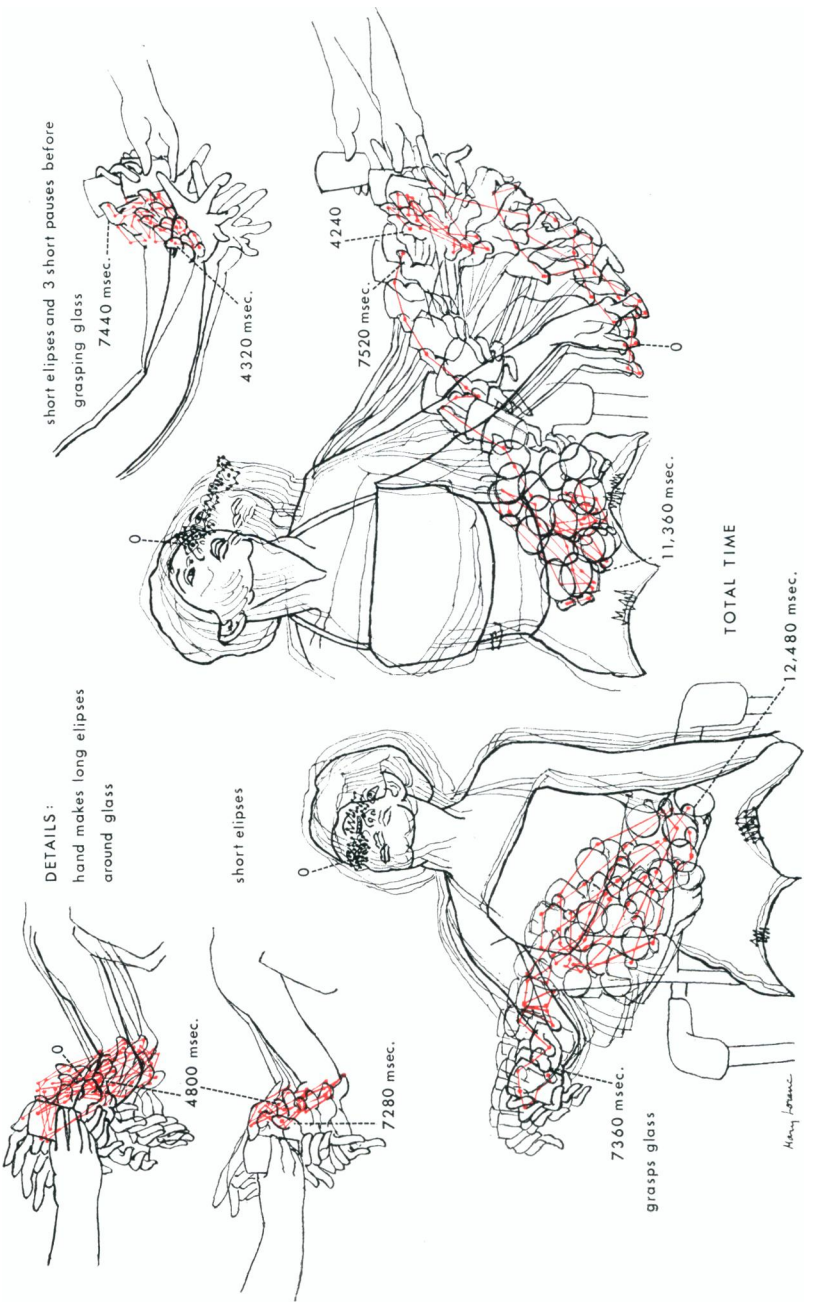


Fig. 12. (*a*) Serial tracings from preoperative cinematographic record of the same patient with Wilson's disease attempting to grasp a glass of water and bring it to her lips. Note the severe bilateral involuntary movements and the total inability of this patient to bring the glass to her lips.

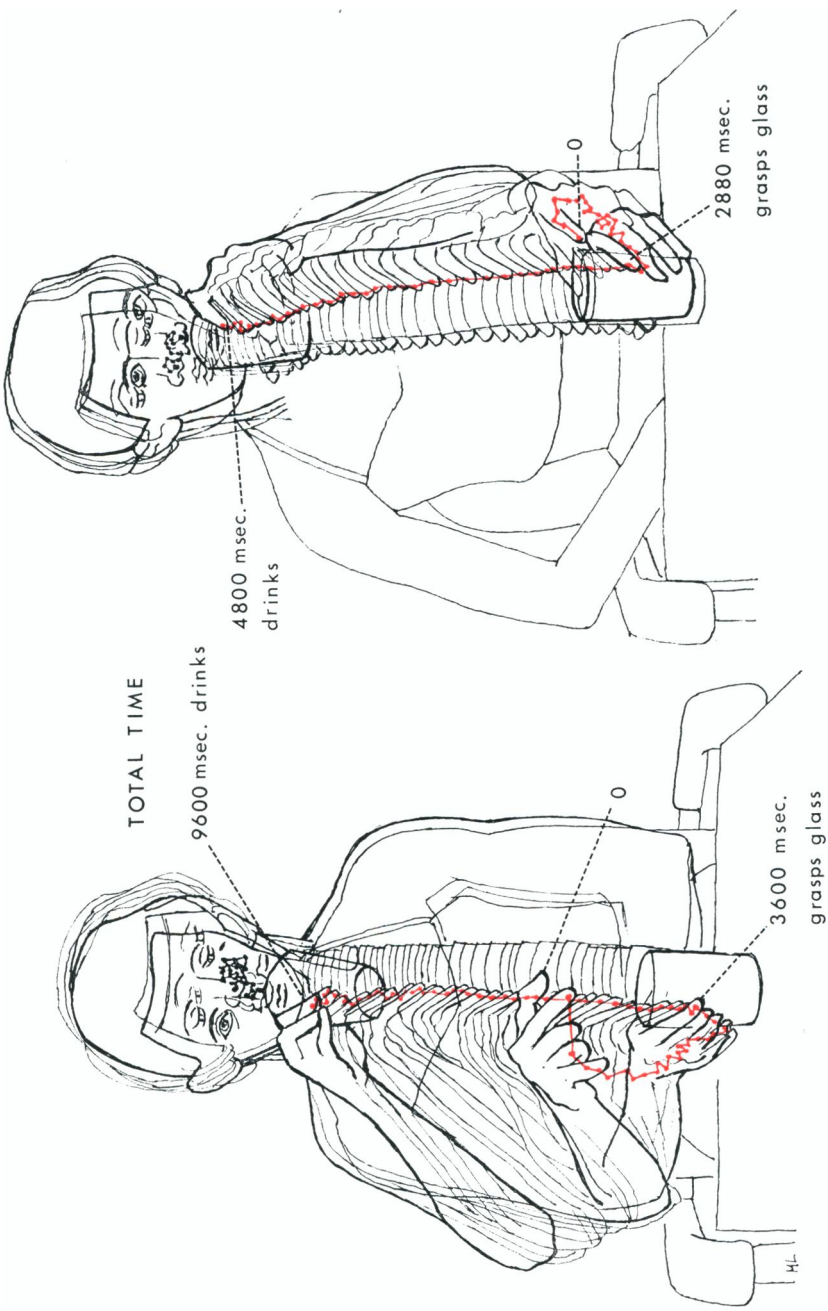
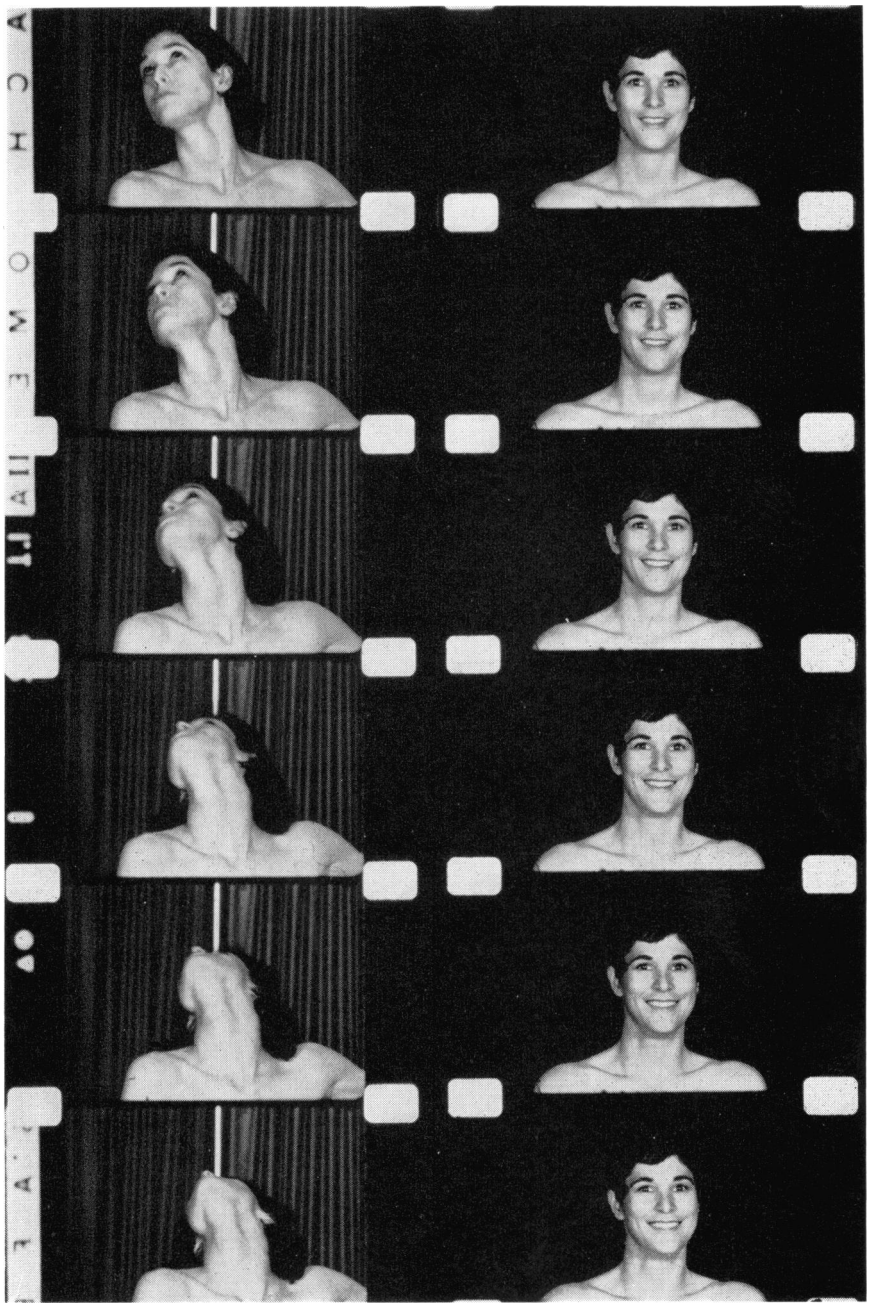


Fig. 12. (*b*) Serial tracings from postoperative cinenatographic record of the same patient 10 months following left chemothalamectomy. Note the profound bilateral abolition of the intention tremor by the left thalamic lesion. This marked ipsilateral as well as contralateral effect is rare, but is worthy of note for its physiologic as well as its clinical significance.

It may be assumed therefore, on the weight of this evidence, that one of the factors underlying hyperkinesis of nuchal musculature in cases of torticollis and retrocollis is failure of the cerebellothalamic servomechanism that modulates somatic motor pathways maintaining the head and neck in its normal position. The spasmodic jerks often accompanying torticollis appear to be attempts to correct this forced abnormal position. It appears that a substitute servomechanism will occasionally serve temporarily to return the head to its normal midline position. For example, many patients whose heads are maintained in an abnormal posture with the chin markedly diverted to one side or the other, and who cannot voluntarily return the chin to the midline position, may often do so and maintain the chin in the midline by placing one finger upon it and gently guiding it back to its normal midline position. I should like to suggest that this is possible because the nerve endings in the finger that has been placed upon the chin become, in effect, the origin of a substitute servomechanism principally proprioceptive in nature that serves to inform central postural mechanisms of the head's position in space.

The most profound favorable effect noted in cases of torticollis or retrocollis in my experience has resulted from lesions involving the ventrolateral and ventroposteromedial nuclei and lateral portion of centrum medianum of the thalamus bilaterally. In some instances, no clinical result is observed until the bilateral operation has been completed, even though the clinical syndrome may appear to be principally a unilateral one. However, in occasional cases the ipsilateral effect may be as profound, or more so, than the contralateral effect, while in rare cases a unilateral lesion may produce bilateral lessening of nuchal hyperkinesis. The text accompanying Figures 13 to 15 cites various cases as examples of the varying contralateral, ipsilateral or bilateral effect of thalamic lesions.

This clinical and electromyographic evidence of varying effects of unilateral and bilateral thalamic lesions, in different cases of torticollis, appears at first to be somewhat paradoxical and confusing. However, it is obvious that lesions in the thalamus on one side of the brain affect the modulation of voluntary and postural muscular activity on both sides of the neck, in varying degrees under different circumstances. Further analysis and experience with these cases may contribute to increase our understanding of normal and pathophysiologic thalamic mechanisms,



(*a*) (*b*)

Fig. 13. (*a*) Cinematographic record of severe dystonic torticollis in a 27-year-old woman.

(*b*) Reversal of torticollis by bilateral therapeutic thalamic surgery. In this case a therapeutic effect was not observed until lesions had been placed in the right and left thalamus.

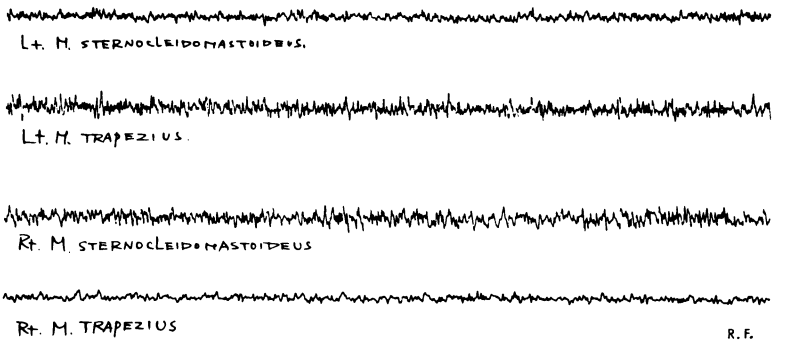


Fig. 14. (*a*) Preoperative electromyogram demonstrating bilateral involuntary muscular activity in a 28-year-old man with torticollis.

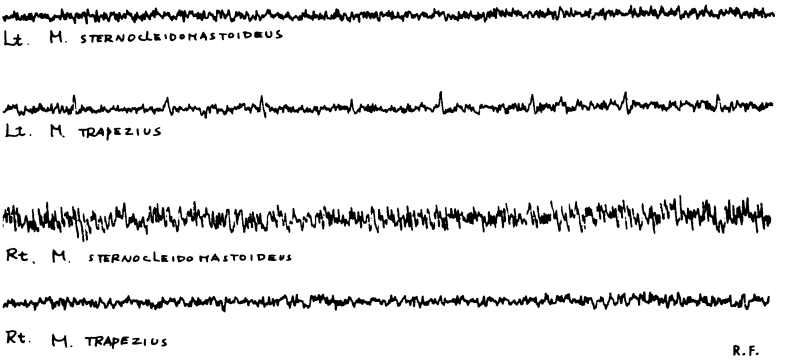


Fig. 14. (*b*) Electromyography following left cryothalamectomy reveals essentially the same tracing as that seen preoperatively.

as well as our understanding of the function of the structures subserving the mechanism of torticollis and related syndromes.

Summary

One may now attempt to tie together the clinical and physiologic observations that have been made during the course of our experience with these four syndromes of hyperkinetic disorders. Intention tremor is determined by a lesion, usually in the brachium conjunctivum, between the dentate nucleus and the red nucleus. Dystonia has, as the sites of principal causative lesions, the caudate nucleus, putamen, brachium conjunctivum, and emboliform nucleus. This is true of the dystonia of Wilson's disease, as well as of dystonia musculorum deformans. The pathologic lesions underlying torticollis have not been established ana-

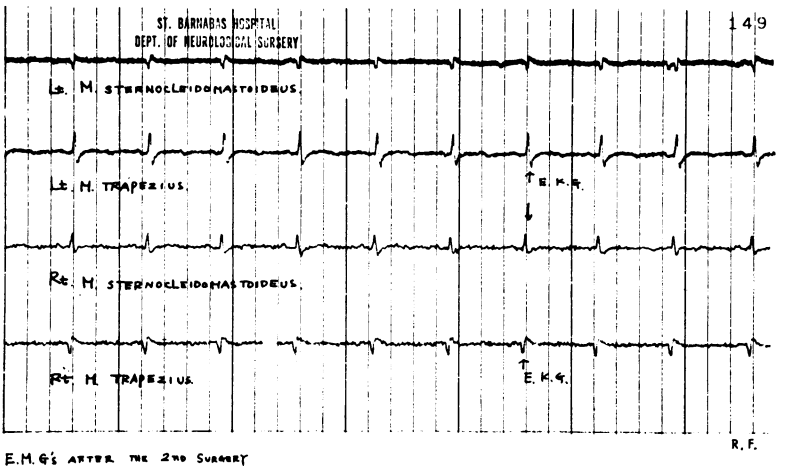


Fig. 14 (*c*) Electromyogram following right cryothalamectomy reveals total absence of involuntary activity.
This is the usual chain of events following thalamic surgery for torticollis. One observes both a contralateral and ipsilateral effect from thalamic surgery, and bilateral surgery is usually required in order to produce a clinical result.

tomically. However, both physiologic and clinical evidence was at hand that helped us to determine the hypothesis that the dentatorubrothalamic pathway subserves, at least in part, the pathophysiologic mechanism of torticollis.

It has been apparent for some years that the various components of the so-called extrapyramidal system, which must include cerebellum as well as the classic basal ganglia, modulate the voluntary motor activity of the corticospinal system by influences upon the cerebral cortex as well as by affecting the descending motor pathways of the brain stem and spinal cord. It has become apparent that facilitatory impulses on any nerve fiber inevitably produce presynaptic inhibition on other neurons as well as sending back presynaptic inhibitory fibers upon itself. In some instances, a particularly strong impulse on one nerve fiber may send back a negative feedback to another neuron, virtually turning off or shutting down the activity of the second neuron. It has been demonstrated that cerebral activity, acting through negative feedbacks at the level of the thalamus, and cuneate nucleus as well as presynaptic inhibition further downstream, can affect proprioceptive and sensory input at the spinal cord level. The thalamus is one of the principal centers producing negative feedback information to the cerebral cortex, principally the motor and premotor areas.

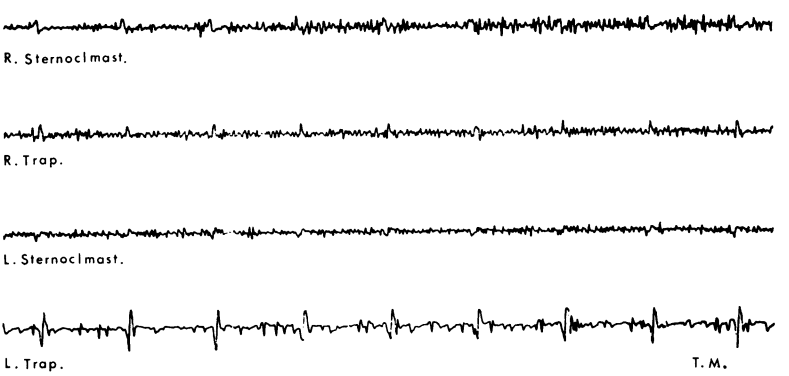


Fig. 15. (*a*) Preoperative electromyographic tracing of a 60-year-old male patient with severe torticollis.

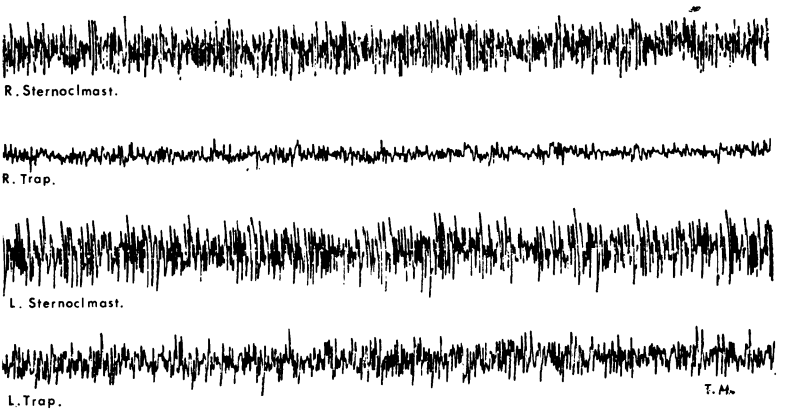


Fig. 15. (*b*) Postoperative electromyogram immediately following left cryothalamectomy.

This illustrates the profound bilateral effect on the cervical musculature from a left thalamic lesion. However, in this patient a total clinical reversal of the syndrome was not observed until the right thalamic lesion was inflicted 10 days later.

Most present investigators agree that impaired or delayed feedback of sensory communication is one of the principal mechanisms productive of hyperkinetic disorders. Dinnerstein[11] postulates that delayed feedback is due to defective muscle spindle pause. Chase[12] has produced stuttering, with both quantitative and qualitative speech defects, by delayed auditory feedback under experimental conditions. Similarly impaired sensory communication probably acts to produce the various components of hyperkinesis demonstrated in this series of cases.

It is the muscle spindles that are now known to be the principal

sensory stretch receptors. They can also be excited by stimulation of their motor fibers. The spindle is a device that signals mechanical events by means of two different outputs, the afferent fibers, and that is controlled by two inputs—the efferent fibers.[13-15]

The main function of the muscle spindle is the role it plays in the nervous control of muscular contraction during movement and during steady state contraction. There is a large projection to the cerebellum of information that is derived directly from the muscle spindles. It is probably for this reason that a cerebellar role in the pathologic mechanism of the four syndromes that we have been discussing is so clearly discernible. It is largely through this pathway that the muscle spindles feed back into the nervous system information concerning the state of the muscles. Obviously, a lesion affecting the circuitry would delay or impair or desynchronize feedback, in such a way as to affect postural and action muscular activity profoundly.

Most of the circuitry concerned with this damping mechanism converges within ventrolateral thalamus and centrum medianum en route to the cortex. Consequently a lesion placed in this area would prevent delayed and impaired feedback from contributing to the production of abnormal muscular activity. Fortunately, enough compensatory mechanisms to provide physiologic safety have been built into this complex afferent system, so that normal motor activity can ensue following the removal of this large source of sensory information from the muscular system. Physiologic explanation of these compensatory mechanisms remains for further elucidation. However, as in many other instances, the central nervous system functions better with the total abolition of this mechanism than with its impaired or erroneous function.

Some liberating concepts that have emerged during the past decade as a result of neurosurgical investigations in hyperkinetic disorders are as follows. First, not only tremor and rigidity but also cerebellar intention tremor, dystonic movements and postures, hemiballismus, and torticollis are capable of reversal without the infliction of motor, sensory, or intellectual abnormality. Second, bilateral large lesions within multiple nuclei of the thalamus can be tolerated to a previously unrealized degree without necessarily affecting any of the basic physiologic, intellectual, or sensory motor activities of man. Third, large lesions may be placed in the sensory projection nuclei, those nuclei directly con-

nected with somesthetic cortex, without necessarily inflicting any substantial degree of objective sensory loss upon the patient. Fourth, such thalamic lesions alone are not apt to produce the so-called thalamic syndrome of intense pain and hyperpathia. Fifth, a lesion of the subthalamic nucleus does not necessarily produce hemiballismus and, conversely, hemiballismus may be produced without the presence of any observable subthalamic lession. Sixth, pain relief is not synonymous with production of analgesia. Seventh, ipsilateral as well as contralateral thalamic influences are of major importance in mechanisms subserving disorders of sensory communication—and, consequently, bilateral thalamic surgery may sometimes be required to relieve a unilateral hyperkinetic or painful syndrome.

One of the most important lessons that I believe an analysis of this type of material offers is the great flexibility and variability of response of specific portions of the central nervous system under varying conditions and in different patients. The effect of a pathologic lesion in any particular brain will depend upon the previous development, aging, and conditioning of that brain. Similarly, the effect of any lesion inflicted for therapeutic purposes will be determined likewise by the underlying condition of that particular nervous network and, particularly, by the conditioning of the specific pathologic process which, in the case of the hyperkinetic disorders and in the case of painful syndromes, is so variable from patient to patient.

During the course of these discussions surgical technique has not been emphasized. However, in keeping with our conclusion that variability and flexibility within the nervous system is the single most important concept with which one deals in inflicting therapeutic lesions, a basic principle that has evolved in the course of our own study deserves mention. That is, it is judicious to inhibit temporarily an intracerebral structure in a conscious, cooperative patient before proceeding to the infliction of a permanently destructive lesion.

The thalamus has apparently held intrigue and interest for investigators for many centuries and undoubtedly owes its name to this fact. The word *talamo* comes from the Greek, and its meaning was connubial couch. Undoubtedly it was apparent to the early investigators that this structure deep within the brain was a hotbed of sensory-motor activity, and they indicated this by naming it the *talamo*—or connubial couch of the brain. The word thalamus is also found in archeological

literature, where it signifies a secret chamber. Thus, whether one explores the thalamus in the original Greek sense, as a hotbed of sensory motor activity or in the archeological sense as a secret chamber, one is following a long line of earlier investigators who found this structure intriguing and mystifying, as we still do today. Although a beginning has been made in unveiling some of its secrets, its form and function are still shrouded in mystery and, like the connubial couch, I believe that it will continue to hold a great allure for neurologic investigators for a long time to come.

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